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Russell C. Johnson, PhD, *Guest Editor*

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Erythema migrans, a red, annular, centrifugally expanding plaque, is the distinctive cutaneous marker of Lyme disease. Its clinical and histopathologic picture may vary considerably. Because the diagnosis of early Lyme disease is primarily a clinical one, recognition of erythema migrans is essential for the institution of appropriate treatment.

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<i>John J. Halperin</i>	

Neurologic involvement is commonplace in Lyme borreliosis. Neuropathies can be acute or chronic, focal or disseminated, but are predominantly axonal. CNS infection can also be acute or indolent, focal or disseminated; meningitis, encephalitis, and cranial nerve palsies occur. A mild encephalopathy is also common, but only occasionally due to CNS infection

<b>Lyme Disease: Musculoskeletal Manifestations .....</b>	<b>649</b>
<i>John Kolstoe and Ronald P. Messner</i>	

Several distinct patterns of musculoskeletal involvement can be seen throughout the course of untreated Lyme disease. Clinically, Lyme arthropathy closely resembles the reactive arthropathies. In a few cases, Lyme disease has mimicked other connective tissue disorders. The full spectrum of musculoskeletal Lyme disease is still being defined.

**Gestational Lyme Borreliosis: Implications for the Fetus ..... 657***Alan B. MacDonald*

Lyme borreliosis shows diverse clinical presentations in the human pregnant patient. The extremes of fetal well being and fetal death mark the ends of the clinical spectrum of gestational Lyme borreliosis. Other more subtle clinical manifestations of gestational Lyme borreliosis are introduced in this review. The shortcomings of serology diagnostic methods are reviewed in the special situation of the maternal fetal setting.

**Lyme Disease in Children ..... 679***Kiran Belani and Warren E. Regelman*

The authors have emphasized the differences between children and adults in the clinical presentation of and therapeutic options available for Lyme disease. The role of serology in the diagnosis of Lyme disease in an endemic area from our experience at the Pediatric Rheumatology Clinic is also described.

**Histopathology of Clinical Phases of Human Lyme Disease ..... 691***Paul H. Duray*

Acute, subacute, or chronic persistent human Lyme borreliosis is an inflammatory disorder composed pathologically of lymphocytes, plasma cells, macrophages, and mast cells. The lymphoplasmocellular infiltrates can at times be seen in the skin, subcutaneous tissues, lymph nodes, spleen, liver, myocardium, brain, autonomic ganglia, and peripheral nerves. The joints in arthritic cases have proliferative synovitis, fibrinaceous deposits, lymphoplasmocellular aggregates, and mast cells. Varying degrees of vascular damage does occur in these sites; however, usually only in late, chronic disease. Spirochetes are present in most sites, in an extracellular location, but are sparse.

**The Pathogenesis of Lyme Disease ..... 711***Juan Carlos Garcia-Monco and Jorge L. Benach*

With the available evidence, persistence of spirochetes in tissues appears to be the most likely mechanism for the pathogenesis of Lyme disease. However, the existence of autoimmune mechanisms need not be excluded as a contributory pathway to tissue damage. This lack of specificity may explain the capacity of Lyme disease to reside in and injure vastly different tissues.

**Immunodiagnosis of Lyme Borreliosis ..... 727***Raymond J. Dattwyler and Benjamin J. Luft*

The clinical definition of Lyme disease depends on the epidemiologic association of signs and symptoms with a measureable immune response to *B. burgdorferi*. The dependence on the demonstration of an immune response to *B. burgdorferi* has made the understanding of this systemic spirochetosis critical for the physician when making a diagnosis.

**Laboratory Diagnosis of Lyme Disease ..... 735***Louis A. Magnarelli*

Of the diagnostic techniques available for the confirmation of *Borrelia burgdorferi* infections, antibody detection assays are the most commonly used. However, antibody responses are quite variable and remain low in some patients. Indirect fluorescent antibody staining methods and enzyme linked immunosorbent assays (ELISA) are often negative when serum specimens are collected from patients within 3 weeks after onset of illness. Improved sensitivity has been reported for a capture ELISA designed to detect IgM antibody during early disease. Immunoblotting techniques have been effectively used along with the conventional antibody methods for laboratory diagnosis. The replacement of sonicated whole cells of *B. burgdorferi* with purified flagellin or selected mixtures of immunogenic proteins of this spirochete as antigen may increase the sensitivity and specificity of ELISA. Serologic tests for antibodies to *B. burgdorferi* are valuable aids in confirming Lyme disease, but standardization of testing among laboratories and technological improvements are needed.

**Treatment of Lyme Borreliosis ..... 747***Benjamin J. Luft and Raymond J. Dattwyler*

The infectious process of Lyme disease can appear as chronic dermatologic, rheumatologic, or neurologic. To rationally select a treatment regimen, the physician must have an appreciation of the clinical manifestations of the illness and of the systemic nature of the infection. The authors discuss the proper treatment protocols for each stage in the progression of Lyme disease.

**Preventing Lyme Disease ..... 757***John F. Anderson*

Collectively, the five *Ixodes* tick vectors of *Borrelia burgdorferi*, which frequently feed on humans, are dis-

tributed over vast areas of Europe, Asia, and North America. Lyme disease is becoming more prevalent in the United States and in Europe because people are increasingly becoming exposed to infected ticks. While numbers of ticks may be reduced locally by chemical, environmental, and possibly by biological means, personal protective efforts taken by the individual to prevent tick bites and to locate and promptly remove attached ticks may be the most effective measures of reducing risk of contracting Lyme disease.

## **Lyme Borreliosis in Europe: Neurologic Disorders ..... 767**

**Wolfgang Kristoferitsch**

In Europe, the tick-transmitted disorders of the peripheral nervous system MPN-GBB or Bannwarth's syndrome and ACA-associated neuropathy have been identified as clinical entities long before their etiologic agent *B. burgdorferi* was detected. Later, when serodiagnostic tests were available, a broad spectrum of CNS disorders was also found to be caused by infection with *B. burgdorferi*. Initially described differences between European and North American cases with neurologic manifestations of Lyme borreliosis became as less prominent as more cases were reported.

## **Vector/Host Relationships of the Lyme Disease Spirochete, *Borrelia burgdorferi* ..... 775**

**Willy Burgdorfer**

Lyme borreliosis is now occurring on several continents where its causative agent, *Borrelia burgdorferi*, is maintained and transmitted by ticks of the "Ixodes ricinus complex" namely *I. dammini*, *I. pacificus*, and possibly *I. scapularis* in North America, *I. ricinus* in Europe, and *I. persulcatus* in Asia. Because all developmental stages of these ticks feed on a large variety of hosts including humans, the vector/host relationships of this spirochete is highly complex as indicated by the voluminous literature reviewed in this article.

The association of *B. burgdorferi* with ticks parasitizing exclusively rabbits and birds, suggests that the geographic distribution of this agent may be far greater than assumed and may include areas where the disease in humans is absent.

Finally, the persistence of the Lyme disease spirochete in the midgut of its tick vectors and its invasion of other tissues during the ticks' feeding, are unique and differ from the behavior of all other arthropod-borne borreliae.



*Special Article***The Use of Antirheumatic Medication During Pregnancy and in the Puerperium ..... 789***Peter M. Brooks and Christopher J. Needs*

The authors provide guidelines for the use of medication during conception, pregnancy, and lactation. In most rheumatic diseases, disease activity can be reduced to a minimum by using the smallest possible doses of drugs with known behaviors during pregnancy and lactation, thus providing minimal risk to the mother and fetus.

**1989 Cumulative Index ..... 807****Subscription Information ..... Inside Back Cover**